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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/556,178	04/20/2000	Olga Bandman	PF-417-US	5936

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EXAMINER
STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
1637	8

DATE MAILED: 04/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/556,178	BANDMAN ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *3-15,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,16,17,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This is a response to an amendment filed on January 31, 2001. The rejections of claims 1, 2, 16 and 17 under 35 U.S.C. 112 are withdrawn, as is the rejection of claims 1 and 2 under 35 U.S.C. 102. The rejection under 35 U.S.C. 101 is maintained.

2. The declaration under 37 CFR 1.132 filed on January 31, 2002 is insufficient to overcome the rejection of claims 1, 2, 16, and 17 based upon lack of utility as set forth in the last Office action. The arguments are presented below.

3. Applicants continue to traverse the restriction to having only one SEQ ID NO examined, namely SEQ ID NO: 1, arguing that in two other applications, now patented (08/967,364 and 09/368,408) claims to polynucleotides encoding SEQ ID NO: 1, 3 and 5 were examined. These patents were examined before the guidelines for the examination of sequences established recently, and therefore Applicants argument is not found persuasive. The requirement is still deemed proper and is therefore made FINAL.

Applicants Arguments

4. For clarity, Applicants' arguments are summarized below. Each section lists arguments which are unique to that section and the sections in which they were reiterated.

A) Inventions have patentable utility as set forth in the specification and/or a utility well-known to one of ordinary skill in the art (A1, page, 8, 9; reiterated on pages 11, 12 of B1)

a) Applicants assert that VTP-1 (vesicle trafficking protein-1) is a member of the vps-45 related family of proteins, whose biological functions include mediating transport among the Golgi complex, synaptic vesicles, prelysosomal compartments, and the lysosome (specification, page 2, lines 2-4), and therefore the invention is useful in toxicology testing,

drug development, and diagnosis of disease, "...none of which require knowledge of how the polypeptide actually functions."(emphasis added)

b) "The similarity of the claimed polypeptide to another polypeptide of known, undisputed utility by itself demonstrates utility beyond the reasonable probability required by law".(emphasis added). VTP-1 is homologous to mouse Vps45 protein, implicated in Golgi to lysosome trafficking, with the two proteins sharing 97% sequence identity over 570 amino acids and "...rather similar hydrophobicity plots". Pevsner et al. (Gene, vol. 183, pp. 7-14, 1996) teaches that "... A description of the proteins involved in lysosomal targeting is essential to understand lysosomal function in the biosynthetic and endocytic pathways, and also to understand diseases involving lysosomes. Protein trafficking to lysosomes may be disrupted in neurodegenerative disorders such as Alzheimer's disease and prion encephalopathies (Mayer et al., 1992; Cataldo et al., 1994) as well as organelle storage disorders diseases such as Chediak-Higashi syndrome (Zhao et al., 1994)" (page 14).

c) The Declaration of L. Michael Furness describes some of the practical uses in gene and protein expression monitoring, in particular, in protein expression analysis such as 2D-PAGE gels and Western blots.

d) The law does not require knowledge of biological function to prove utility. "It is the claimed invention's uses, not its function, that are the subject of proper analysis under the utility requirement....the person of ordinary skill in the art can achieve beneficial results from the claimed polypeptide in the absence of any knowledge as to the precise function of the protein. ."(emphasis added). The uses of the claimed polypeptide for gene expression monitoring applications including toxicology testing are in fact independent of its precise function."

B) The uses of VTP-1 for toxicology testing, drug discovery, and disease diagnosis are sufficient utilities under 35 U.S.C. 101 and 112, first paragraph. (B1, pages 13-19).

a) Homology in excess of 40% over 70 or more amino acid residues yields a high probability of functional homology as described in Brenner et al. (PNAS USA, vol. 95, pp. 6073-78, 1998). The known art (Russel et al., Gerhold et al, Wells et al.) "...clearly demonstrates that evolutionary related proteins may exhibit considerable divergence in sequence while conserving the same overall three-dimensional structure and function." (emphasis added).

b) The Revised Utility Guidelines at page 1096 state "...that the Examiner's decision to rebut Applicants assertion of utility:

---must be supported by a preponderance of all evidence of record. More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the Examiner unless the office has sufficient evidence or scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient". (emphasis added)." The Applicants further describe an example about sequence homology to a ligase.

c) "The claimed invention has specific, substantial, real-world utility by virtue of its use in toxicology testing, drug development and disease diagnosis through gene expression profiling". In particular, the polypeptides are useful in 2D-PAGE electrophoresis used as a tool in toxicology and drug efficacy testing, which are now well-established in

pharmaceutical industry. Other real-world uses are commercial uses of the invention, such as databases of genetic information.

C) The Patent Examiner's Rejections are Without Merit (pages 19-24).

a) Biological role or function is not required to demonstrate utility. "Knowledge of the biological function or role of a biological molecule has never been required to show real-world benefit. In its recent explanation of its own utility guidelines, the PTO acknowledged as much (66 F.R. at 1095):

[T]he utility of claimed DNA does not necessarily depend on the function of the encoded gene product. A claimed DNA may have specific and substantial utility because, e.g., it hybridizes near a disease-associated gene or it has gene-regulating activity. By implicitly requiring knowledge of biological function for any claimed polypeptide, the Examiner has, contrary to law, elevated what is at most an evidentiary factor into an absolute requirement of utility. Rather than looking to the biological role or function of the claimed invention, the examiner should have looked first to the benefits it is alleged to provide" (emphasis added).

b) Membership in a class of useful products can be proof of utility (some of the arguments are reiterated here). "As demonstrated by Applicants, knowledge that VTP-1 is a Vps45-related protein and an expressed polypeptide is more than sufficient to make it useful for the diagnosis and treatment of inflammation and disorders associated with cell proliferation and apoptosis. Indeed, VTP-1 has been shown to be expressed in tissues associated with cancer, inflammation and fetal/infant development. (Specification, page 27, lines 27-29). The Examiner must accept these facts to be true unless the Examiner can provide evidence or sound scientific reasoning to the contrary." (emphasis added).

c) The uses of VTP-1 in toxicology testing, drug discovery, and disease diagnosis are practical uses beyond mere study of the invention itself (arguments reiterated).

D) By Requiring the Patent Applicant to Assert a Particular or Unique Utility, the Patent Examination Utility Guidelines and Training Materials Applied by the Patent Examiner Misstate the Law. (pages 24-26).

The Applicants argue that Patent Examination Utility Guidelines and Training Materials are inconsistent with the law.

Summarizing, Applicants argue that the VTP-1 polypeptide has a specific and substantial utility by virtue of being homologous to mouse Vps45 polypeptide and has a well-established utility by being useful in toxicology testing, drug discovery and disease diagnosis.

Response to Arguments

I. Specific and Substantial Utility.

The instant application has provided a description of an isolated DNA encoding a protein, VTP-1, and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. The instant specification asserts that it provides compositions that may be used for stimulation of cell proliferation, prevention and treatment of disorders associated with an increase in apoptosis, cancer and inflammation (see specification at page 4, lines 4-14). The specification asserts that the polynucleotides encoding VTP sequences can be used for the diagnosis of conditions or disorders which are associated with expression of VTP, "disorders associated with cell proliferation, such as adenocarcinoma, leukemia, lymphoma, melanome, myeloma, sarcoma, and teratocarcinoma and particularly cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis,

thymus, thyroid, and uterus; disorders associated with inflammation such as Addison's disease, adult respiratory distress syndrome, allergies, anemia, asthma, atherosclerosis, bronchitis, cholecystisis, Crohn's disease, ulcerative colitis, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, atrophic gastritis, glomerulonephritis, gout, Grave's disease, ...; complications of cancer, hemodialysis, extracorporeal circulation; viral, bacterial, fungal, parasitic, protozoal, and helminthic infections and trauma; disorders with associated apoptosis such as ADIS and other infectious or genetic immunodeficiencies, neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, and cerebellar degeneration, myelodisplastic syndromes such as aplastic anemia, ischemic injuries such as myocardial infarction, stroke, and reperfusion injury, toxin-induced diseases such as alcohol-induced liver damage, cirrhosis and lathyrism, wasting diseases such as cachexia, viral infections such as those caused by hepatitis B and C, and osteoporosis." (specification, page 39, lines 28-30; page 40, lines 1-24).

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the VTP-1 protein of the instant invention. The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins, namely, the Vps45 yeast and mouse proteins. After further research, a specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the VTP-1 of the instant application was, as of the filing date, useful for diagnosis,

prevention and treatment of apoptosis-related disorders, cancer and inflammation, as stated at pages 4, 39 and 40 of the specification. The only link provided in the specification between the VTP-1 protein and the disorders is the fact that VTP-1 has been shown to be expressed in tissues associated with cancer, inflammation and fetal/infant development (Specification, page 27, lines 27-29). The types of tissues or their sources are not disclosed, and there is no evidence provided that there is a difference in the level VTP-1 expression as compared with normal tissues. Until some actual and specific significance can be attributed to the protein identified in the specification as VTP-1, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention.

In order for a polypeptide to be useful for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a disease or disorder. The presence of a polypeptide in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed cDNA and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed

polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Applicants argue that assertion of utility based on homology to existing protein having an accepted utility must be accepted by the examiner. The evidence present in scientific literature so far fails to point to utility for the mouse Vps45 protein. In addition to the Pevsner et al. reference cited in the Office action, which does not provide a role for the Vsp45 protein, only a hypothesis for its role, additional references related to the Vsp45 proteins were examined. These references are:

1. Piper, R.C. et al., Europ. J. Cell Biology, vol. 65, pp. 305-318 (1994).

2. Pevsner, J., J. Neurosci. Res., vol. 45, pp. 89-95 (1996).

3. Tellam, J. T. et al., J. Biol. Chem., vol. 272, pp. 6187-6193 (1997).

4. El-Husseini A. E-D. et al., BB Acta, vol. 1325, pp. 8-12 91997).

5. Rajasekariah. P. et al., Int. J. Biochem. & Cell Biol., vol. 31, pp. 683-694 (1999).

The following facts concerning the role of Vsp45 proteins have been established by these references:

1. Vsp45 protein in yeast is one of over 45 genes which control the delivery of soluble hydrolases from the yeast Golgi to the vacuole/lysozyme. It is a peripheral membrane protein, and mutations in Vps45 cause accumulation of small vesicles and secretion of the vacuolar hydrolase carboxypeptidase Y (Abstract, p. 309-312).

2. The role in vesicle trafficking and subcellular localization of the mammalian Vps45 (mVps45) has not been established (page 92, first paragraph).

3. Expression of mVps45 in rat tissues was detected mainly in the brain, testis and fibroblasts, but at lower levels also in liver, kidney, intestine, heart, muscle, fat, and adipocytes (Fig. 2). mVps45 is a peripheral membrane protein. "Genome sequencing efforts in S. pombe and C. elegans have also described analogs of Vps45p on the basis of predicted protein sequences (45). Exactly what membrane trafficking steps the various Vps45 proteins catalyze and with what proteins they interact are central questions." (page 6192, fifth paragraph). (emphasis added).

4. Rat homologue of vps45, rVps45, was identified and cloned. Northern blot analysis of rVps45 mRNA showed expression in liver, lung, testis, heart, spleen, kidney, muscle, cerebellum and brain, with the highest expression levels in the brain and testis (Abstract, Fig. 3). The exact role and subcellular localization of rVps45 are not know. "The identification of the mammalian rvps45 will provide us with the tools to determine the role of this protein in mammalian secretory pathways. In particular, the high expression of this protein in the brain suggests that rvps45 could play an important role in synaptic vesicle trafficking and neurotransmission". (emphasis added).

5. A new variant of human Vps45 protein has been cloned and characterized (h1Vps45). It has 90% sequence homology to the human Vps45 protein. It is expressed in a variety of tissues, with the strongest expression in heart, spleen, testis, neutrophils and peripheral blood mononuclear cells. (Abstract; Fig. 2-4; Table 1). The presence of h1Vps45 and Vps45 in human tissue samples suggests a multigene family (page 693, first paragraph). "Further insight into the exact function of h1Vps45 will be achieved by studying in vitro binding of

h1Vps45 to any known syntaxins in order to establish its functional role as well as its relation with other Golgi proteins" (page 693).

Therefore, from the point of view of references 1-5 and Pevsner et al., VTP-1 cannot have a specific and substantial utility based on its homology to the other mVps45 proteins, since the biological significance of these proteins is not known and require further investigation.

To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for VTP-1, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

II. Well-established Utility

Applicants argue that the claimed polynucleotides and polypeptides are useful as tools for toxicology testing, drug discovery, and the diagnosis of disease and that these uses are "well-established". It is noted that toxicology testing and drug discover are not specifically recited in the specification as originally filed. Each of these uses will be addressed individually, because the facts and issues directed to each use are distinct and separable.

First, Applicants argue that toxicology testing is a well-established utility and conclude that the claimed polypeptides could be used in this manner and that the claimed invention possesses utility. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case, all polypeptides are in some combination useful in toxicology testing using 2D-PAGE electrophoresis. However, the particulars of toxicology testing with SEQ ID NO:1 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general

class of materials, such as any collection of proteins, but is only potential with respect to SEQ ID NO:1. Because of this, such a utility is not specific and does not constitute a "well-established" utility.

Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polypeptide in 2D-PAGE electrophoresis for toxicology screening is only useful in the sense that the information that is gained from the gels is dependent on the pattern derived from the gels, and says nothing with regard to each individual protein spot on the gels. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins.

Even if the expression of Aplicants' individual polypeptide is affected by a test compound for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this polypeptide could be put.

With regard to drug discovery and development, Aplicants mention expression profiling as one use of the claimed polypeptide, with 2D-PAGE electrophoresis as a method for quantifying the relative expression levels of a large number of proteins within a biological sample. In this manner, a protein expression profile is generated. Such a profile is independent of the function of the proteins. In the instant case, the claimed polypeptides can be used as one of many proteins in the 2D-PAGE gel map.

In addition, the efficacy (ability of producing a desired effect) of a drug compound could not be evaluated from the 2D-PAGE gel map because there is no way to assess the meaning of any individual hit obtained from this procedure. The first requirement is that one must know the biological significance of the polypeptide(s) which is(are) being evaluated. Without this information, the results of the 2D-PAGE gel map are useless because one would not know if the polypeptide expression should be increased or decreased or even what significance could be attributed to such changes in expression profiles. Applicants cite Wilkins et al. (Biotechnology and Gen. Eng. Reviews, vol. 13, pp. 19-50, 1995) stating that the aim of the 2D gel analysis is to catalogue all spots from the 2-D gel in a qualitative and/or quantitative manner to define the number of proteins and their expression, to be potentially useful as reference gel images in 2-D gel image database (page 26, third paragraph). However, this is again points to a broad utility of SEQ ID NO: 1 as one of the proteins in the image, not specifically to the utility of SEQ ID NO: 1.

In conclusion, Applicants failed to document well-established utility for SEQ ID NO: 1.

By Requiring the Patent Applicant to Assert a Particular or Unique Utility, the Patent Examination Utility Guidelines and Training Materials Applied by the Patent Examiner Misstate the Law.

Examiner's role is to examine applications with the direction of rules and guidelines established by the Patent Office. Whether such rules and guidelines are lawful or not is to be determined by the courts.

35 U.S.C. 101 Utility Rejections

5. The pending claims have been reviewed in light of the the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph,

□Written Description□ Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant□s assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

1. 35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

2. Claims 1, 2, 16, 17, 21 and 22 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well established utility.

The claimed polypeptide compound (VTP-1, SEQ ID NO: 1) is not supported by a specific asserted utility because the disclosed uses of the protein are not specific and are generally applicable to a wide variety of proteins. The specification states that the nucleic acid compounds encoding

VTP-1 may be useful as hybridization probes, PCR primers, in microarray assays, gene mapping, for therapeutic purposes as antisense ologonucleotides, parts of expression vectors and for gene therapy (page 32 lines 10-30; page 33; page 34, lines 1-22; page 38, line 31; page 39-44; page 45, lines 1-19). Similarly, protein may be used for detection of expression, antibody production, Western blots, and therapeutic application against a wide range of conditions (disorders associated with increased apoptosis, cell proliferation, inflammation) (page 28-30; page 31, lines 1-9; page 38, lines 13-30; page 45, lines 20-30; page 46, lines 1-7). These are non-specific uses that are applicable to nucleic acids and/or proteins in general and not particular or specific to the nucleic protein being claimed.

Further, the claimed protein compound is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the protein compound such that another non-asserted utility would be well established for the compounds.

It is noted that applicants have listed a sequence which is known in the prior art (human homologoue of a yeast vacuolar protein sorting vps45) and which has a 97.8% sequence similarity to a claimed sequence (VPT-1). Absent factual evidence, a percentage sequence similarity of less than 100 % is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single

nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Gerhold et al. (BioEssays, Volume 18, Number 12, pages 973-981, 1996); Wells et al. (Journal of Leukocyte Biology, Volume 61, Number 5, pages 545-550, 1997); and Russell et al. (Journal of Molecular Biology, Volume 244, pages 332-350, 1994).

In addition, the function of human vps45 protein is not known. Pevsner et al. (Gene, vol. 183, pp. 7-14, 1996) teaches that human vps45 homologue may participate in vesicular trafficking between the Golgi and the lysosome and may interact with syntaxin homologues which potentially mediate specific stages of vesicle trafficking, but they conclude that the function of this protein is unknown. This protein does not bind to the known syntaxins (page 7; page 8, second paragraph; Fig. 3 and Table 1; page 13, second and third paragraphs). Therefore, it is not possible to ascertain at present what is the utility of VTP-1, and thus, what disorders may be treatable with this polypeptide.

Claims 1, 2, 16, 17, 21 and 22 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible

utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

TS
March 12, 2002 TS

Kenneth R. Horlick
KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
3/13/02